Pancytopenia

All three lineages down · Decide today whether the marrow is empty, replaced, or being destroyed

FILM FIRST
blasts change everything

TRIAGE BEFORE YOU INVESTIGATE *three things must happen in the first hour*

LOOK AT THE FILM

Request an urgent blood film and speak to the hematologist. Blasts mean acute leukemia and change the plan the same day. Schistocytes mean a microangiopathy. **Hypersegmented neutrophils** point to B12 or folate deficiency, which is fully reversible. A **leukoerythroblastic film** means marrow infiltration or fibrosis.

IS THE PATIENT SEPTIC?

Neutropenia plus fever is an emergency regardless of how well the patient looks. **Give broad-spectrum antibiotics within an hour** of recognition, after cultures but never delayed for them. Neutropenic patients mount few localizing signs, so the examination is often unremarkable right up until decompensation.

IS THERE BLEEDING?

Assess for **mucosal, retinal and intracranial bleeding**. Check the **coagulation screen and fibrinogen**: **pancytopenia with a coagulopathy raises acute promyelocytic leukemia**, where early hemorrhagic death is the main risk and **differentiation therapy is started on clinical suspicion, before cytogenetics return**.

TWO MECHANISMS, THEN THE CAUSES *the reticulocyte count separates them cheaply*

Mechanism	Detail
Underproduction	**Low reticulocytes.** The marrow is **empty (aplastic), replaced (infiltrated or fibrotic), dysplastic, or lacking substrate**. This is the group that usually needs a bone marrow examination to resolve.
Destruction or sequestration	**Reticulocytes preserved or high.** Cells are made but consumed — **hypersplenism, immune destruction, microangiopathy, or hemophagocytosis**. The marrow may be normal or hypercellular.
Drugs	**Review every drug and stop the culprit — the highest-yield reversible cause.** Chemotherapy and methotrexate predictably; and idiosyncratically **methimazole, clozapine, TMP-SMX, linezolid, azathioprine, sulfasalazine and chloramphenicol**. Ask about alcohol, which suppresses the marrow directly and causes deficiency. **Recovery after withdrawal of the drug typically takes 1 to 3 weeks**, so a count that has not moved in 48 hours does not exonerate the drug.
Infection	**HIV (test everyone), EBV, CMV, parvovirus B19, hepatitis viruses, tuberculosis, visceral leishmaniasis**, and **overwhelming sepsis itself**. Several are curable or treatable and are missed when the workup jumps straight to the marrow.
Nutritional	**B12 and folate deficiency can produce a full pancytopenia** with a raised LDH and bilirubin that mimics hemolysis. **Cheap to test and completely reversible**, so exclude it before anything invasive.
Marrow and immune	**Acute leukemia, myelodysplasia, myeloma, lymphoma, myelofibrosis, metastatic infiltration, aplastic anemia**; and **lupus, paroxysmal nocturnal hemoglobinuria and hypersplenism from cirrhosis and portal hypertension**. **Myelodysplasia is easily missed in the older patient**, where a slowly falling count is often written off as age or chronic disease.

THE WORKUP *blood tests first, then the marrow*

1. **Confirm it is real and repeat the count.** Check for a clotted or dilute sample, and review previous counts — a long-standing stable mild pancytopenia behaves very differently from a new one.
2. **First-line labs: film and reticulocytes, B12 and folate, liver and renal function, LDH, ferritin, coagulation screen with fibrinogen, immunoglobulins with serum electrophoresis, HIV and viral hepatitis serology, EBV, CMV and parvovirus, autoimmune screen, and a direct antiglobulin test**.
3. **Examine and image for the spleen and nodes. Splenomegaly shifts the differential decisively** towards sequestration, lymphoproliferative disease and portal hypertension. Look for stigmata of chronic liver disease.
4. **Think of hemophagocytic lymphohistiocytosis** when there is **fever, cytopenias and splenomegaly with a strikingly high ferritin**, plus raised triglycerides and a low fibrinogen. **It is rapidly fatal and frequently missed** because each feature is individually attributed to sepsis.
5. **Bone marrow aspirate and trephine** when the cause is not obvious from the blood tests, and **urgently if blasts are present, if there is no reversible cause, or if the counts are severe**. **Do not start corticosteroids before the marrow is sampled** — partially treating an underlying lymphoma or leukemia obscures the diagnosis and can delay definitive therapy for weeks.

SUPPORTIVE CARE WHILE YOU WAIT *what to do before the diagnosis lands*

PROTECT

Neutropenic precautions and prompt antibiotics for any fever. Transfuse platelets by threshold and bleeding, not reflexively, and **use irradiated components where a lymphoproliferative disorder or transplant is possible**. Avoid **intramuscular injections, NSAIDs, aspirin and rectal examinations** in the severely thrombocytopenic. Discuss **fertility preservation early** if leukemia or lymphoma is likely — the window closes once treatment starts.

REVERSE WHAT YOU CAN

Stop every plausible culprit drug and document why. **Replace B12 and folate** if deficient, remembering to **give B12 before folate**. Treat alcohol withdrawal and nutritional deficiency. **Correct the coagulopathy** and treat any identified infection. Many patients improve substantially on these measures alone, and the ones who do not have declared that they need the marrow examination.

PEARLS & PITFALLS

- **Platelet thresholds:** transfuse prophylactically below **10 ×10⁹/L**, below **20** with fever or sepsis, below **50** for an invasive procedure or active bleeding, and below **100** for CNS or ocular bleeding.
- **The smear is the cheapest and fastest test you have.** Blasts, schistocytes, dysplasia or a leukoerythroblastic film redirect the entire workup within minutes, long before the marrow result returns.
- **Get the film reported today.** Blasts, schistocytes or hypersegmented neutrophils each redirect the entire workup.
- **Fever with neutropenia is antibiotics within the hour**, regardless of how well the patient appears.
- **Test for HIV and check B12 and folate in everyone.** Both are cheap, common and completely reversible.
- **Do not give steroids before the marrow is sampled** — it can mask a lymphoma and delay the diagnosis.
- **Pancytopenia with coagulopathy suggests acute promyelocytic leukemia.** Treat on suspicion; the early deaths are hemorrhagic.
- **A very high ferritin with fever and splenomegaly is HLH until excluded**, not simply an acute phase response.

References: BSH guidelines on the diagnosis and management of aplastic anemia · BSH guidance on the investigation of unexplained cytopenias · national neutropenic sepsis standards · HLH-2004 diagnostic criteria and subsequent consensus guidance.

Educational aid; verify against local hematology protocol and patient factors.